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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,254	10/13/2000	Harry M. Meade	GTC-43	9900

31904 7590 12/22/2005
GTC BIOTHERAPEUTICS, INC.
175 CROSSING BOULEVARD, SUITE 410
FRAMINGHAM, MA 01702

EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 12/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/688,254

Applicant(s)

MEADE ET AL.

Examiner

Celine X. Qian Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-25, 27-30 and 43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-25, 27-30 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 November 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 21-25, 27-30 and 43 are pending in the application.

This Office Action is in response to the Amendment filed on 10/21/05.

Response to Amendment

The rejection of claims 21-25, 27-30 and 43 under 35 U.S.C. 112 1st paragraph has been withdrawn.

The rejection of claim 25 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claim.

The rejection of claims 21-25, 27-30 and 43 under 35 U.S.C. 103 (a) is maintained for reasons set forth of the record mailed on 4/20/05 and further discussed below.

Response to Arguments

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 21-25, 27-30 and 43 rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (5,981,714), in view of Radford et al. (5,955,270), Scharwz et al. (5,719,269), Wagner et al. (6,329,209), Meade et al. (5,750,172), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807).

In response to this rejection, Applicants argue that the prior art fails to meet the criteria to establish prima facie obviousness of the claimed invention because they fail to provide motivation and expectation of success to make the claimed invention. Applicants assert that Cheng et al. does not provide for altering the sequence of transgenically produced molecule, does not discuss fusion proteins, does not discuss multivalent binding moieties, and does not discuss

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any modifications to the structure or amino acid sequence of an antibody or other polypeptide, thus fails to render obvious the invention and make itself available for combination as anything resembling analogous art. Moreover, Applicants argue that Cheng et al. fails to provide or teach a) a milk or similar bodily derived substance; b) purification of a transgenically derived molecule using a second transgenically derived molecule; or c) modifying a polypeptide sequence to make purification easier through the use of known binding domains. Applicants point out that the above deficiencies are not remedied by the piecemeal application of the other citations.

Applicants further assert that there is no reason to combine the references because they are not analogous art, wherein one is purification/chromatography/solution procession, and the other is transgenic molecular biology/genetic engineering. Furthermore, Applicants attacks the Schwartz reference for lack of teaching of manipulation of transgenic mammals or the direct alteration of target polypeptides for later biologic production and final production in milk or biologically derived liquid feed stream. Applicants assert that Schwartz is a non-analogous art thus unavailable for combination. Applicants present similar argument with regard to Radford et al. Applicants assert that Radford et al. does not disclose a multivalent polypeptide, transgenic mammalian production, or elution of these molecules from a biologically derived feed stream. Applicants further assert Wagner, Meade, and Nuijens also fail to provide remedies to the above deficiency. Applicants thus conclude that the instant invention, drawn to a novel structural method, transgenic production and a different method of polypeptide purification, is not obvious in view of the prior art since the skilled in the art have not adopted the present invention.

The above arguments have been fully considered but deemed unpersuasive. The reasons for the obviousness of the instantly claimed inventions were set forth in detail in the previous

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office action. Applicants are reminded the claims 21-24 are drawn to a method of obtaining a target polypeptide having a bindable epitope from a product by binding the target polypeptide with a multivalent bindable polypeptide comprising one moiety that binds to the target polypeptide and another moiety that binds to a matrix. The claimed method does not recite any of the following limitation: a) a milk or similar bodily derived substance; b) purification of a transgenically derived molecule using a second transgenically derived molecule; c) modifying a polypeptide sequence to make purification easier through the use of known binding domains; or d) fusion protein. As such, in response to applicant's argument that the references fail to show the above mentioned features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, as discussed in the previous office action, during recited purification process, whether the multivalent protein is produced transgenically or by other means does not impart a structural or functional difference for said protein, as long as it binds the target polypeptide and a matrix. Contrary to Applicant's assertion, the antibody that binds the matrix is structurally and functionally same as the multivalent protein because it has a moiety that binds the matrix and another moiety binds the antigen. Therefore, there is no deficiency for the Cheng reference in teaching the limitation of the claims. Although claims 25, 27-30 and 43 mentions milk as the reaction mixture, the process of which the protein is purified does not differ from the process of purifying the polypeptide from other reaction mixture, such as taught by Cheng et al. Meade et al. teach the a number of proteins produced in the milk of transgenic animal, and demonstrates reasonable expectation of

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success to produce the multivalent protein as claimed. It is unreasonable to separate the art of protein purification from the art of producing exogenous protein in the milk of transgenic animals as non-analogous since such art is closely related because the exogenous protein produced in the milk of the transgenic animal would need to be purified from milk before further use. The purification method known in the art, as demonstrated by Cheng et al, Schwartz et al., Wagner, Radford, and Nuijens can be employed for such purification. Absent evidence from the contrary, one of ordinary skill in the art would have reasonable expectation of success to make the invention as claimed. Since Cheng et al. do not have the alleged deficiencies for reasons discussed above, the remaining reference does not need to remedy such deficiency. Therefore, for reasons discussed in the previous action and above, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777.

The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
PATENT EXAMINER

